

From the INTERNATIONAL BUREAU

**PCT**

NOTIFICATION CONCERNING  
TRANSMITTAL OF COPY OF INTERNATIONAL  
PRELIMINARY REPORT ON PATENTABILITY  
(CHAPTER I OF THE PATENT COOPERATION  
TREATY)

(PCT Rule 44bis.1(c))

To

WHITE, John, P.  
COOPER & DUNHAM LLP  
1185 Avenue of the Americas  
New York, NY 10036  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

26 March 2009 (26.03.2009)

Applicant's or agent's file reference

75415-A-PCT/JPW/YC

**IMPORTANT NOTICE**

International application No.

PCT/US2006/042739

International filing date (day/month/year)

31 October 2006 (31.10.2006)

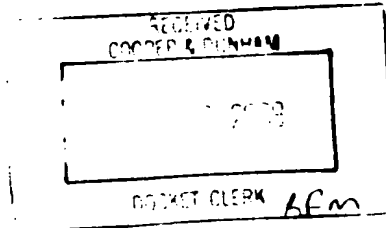
Priority date (day/month/year)

31 October 2005 (31.10.2005)

Applicant

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty).



IDS BASED ON SEARCH 6/17/09  
(75415-A Pct-US)

The International Bureau of WIPO  
44, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Athine

Applicant: Jingyue Ju  
Serial No.: 10/591,520  
Filed: June 4, 2007  
Exhibit 14

Facsimile No.: +41 22 338 82 70

e-mail: p04.pct@wipo.int

**PCT**

NOTIFICATION CONCERNING  
TRANSMITTAL OF COPY OF INTERNATIONAL  
PRELIMINARY REPORT ON PATENTABILITY  
(CHAPTER I OF THE PATENT COOPERATION  
TREATY)

(PCT Rule 44bis.1(c))

From the INTERNATIONAL BUREAU JPW/LCM BT

To:

WHITE, John, P.  
COOPER & DUNHAM LLP  
1185 Avenue of the Americas  
New York, NY 10036  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

26 March 2009 (26.03.2009)

Applicant's or agent's file reference

75415-A-PCT/JPW/YC

**IMPORTANT NOTICE**

International application No.

PCT/US2006/042739

International filing date (day/month/year)

31 October 2006 (31.10.2006)

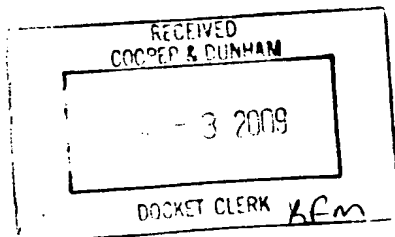
Priority date (day/month/year)

31 October 2005 (31.10.2005)

Applicant

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)



IDS BASED ON SEARCH 6-1709  
(75415-A-PCT-US)

IDS rev. 5/17/09  
due 6/17/09 LCM

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Athina P

Facsimile No. +41 22 338 82 70

e-mail: pt04.pct@wipo.int

DE  
Copies: 3004 (2004)  
LCM (2004)

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 75415-A-PCT/JPW/YC	<b>FOR FURTHER ACTION</b> See item 4 below	
International application No. PCT/US2006/042739	International filing date ( <i>day/month/year</i> ) 31 October 2006 (31.10.2006)	Priority date ( <i>day/month/year</i> ) 31 October 2005 (31.10.2005)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).	
2.	This REPORT consists of a total of 4 sheets, including this cover sheet.  In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.	
3.	This report contains indications relating to the following items:	
	<input checked="" type="checkbox"/> Box No. I	Basis of the report
	<input type="checkbox"/> Box No. II	Priority
	<input type="checkbox"/> Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
	<input type="checkbox"/> Box No. IV	Lack of unity of invention
	<input checked="" type="checkbox"/> Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<input type="checkbox"/> Box No. VI	Certain documents cited
	<input type="checkbox"/> Box No. VII	Certain defects in the international application
	<input type="checkbox"/> Box No. VIII	Certain observations on the international application
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 338 82 70	Date of issuance of this report 17 March 2009 (17.03.2009)
	Authorized officer  <b>Athina Nickitas-Etienne</b>  e-mail: pt04.pct@wipo.int

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
JOHN P. WHITE  
COOPER & DUNHAM LLP  
1185 AVENUE OF THE AMERICAS  
NEW YORK, NY 10036

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) **06 FEB 2008**

Applicant's or agent's file reference

75415-A-PCT/JPW/YC

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

PCT/US06/42739

International filing date (day/month/year)

31 October 2006 (31.10.2006)

Priority date (day/month/year)

31 October 2005 (31.10.2005)

International Patent Classification (IPC) or both national classification and IPC

IPC: C12Q 1/68( 2006.01); C07H 21/04( 2006.01)

USPC: 435/6;536/24.33

Applicant

THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this opinion

21 January 2008 (21.01.2008)

Authorized officer

*Helicia D. Roberts*  
Young J. Kim

Telephone No. (571) 272-1600

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US06/42739

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
- ☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
- ☐ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US06/42739

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims <u>28-30</u>	YES
	Claims <u>1-27, 31, and 32</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-32</u>	NO
Industrial applicability (IA)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and explanations:**

Claims 1-27, 31, and 32 lack novelty under PCT Article 33(2) as being anticipated by Ruparel et al. (PNAS, April 26, 2005, Vol. 102, No. 17, pages 5932-5937).

Ruparel et al. disclose a nucleotide analog comprising a 3' modification, wherein said modification is an allyl moiety bound to the 3'-oxygen of the nucleotide, and fluorophore bound via an allyl linker (page 5933, 2<sup>nd</sup> column, 3<sup>rd</sup> paragraph).

With regard to claims 2-6, the nucleotide analog is 3'-O-allyl-dUTP-PC-Bodipy-FL-510 (page 5933, 2<sup>nd</sup> column, bottom paragraph).

With regard to claims 7-18 and 31-32, Ruparel et al. disclose the method of synthesizing the above modified nucleotide analog (page 5933, 2<sup>nd</sup> column, bottom paragraph, to page 5933, 1<sup>st</sup> column, 1<sup>st</sup> paragraph).

Ruparel et al. also disclose the method of making an oligonucleotide bearing the 3'-O-allyl-modification, the modification being made at the thymidine residue (page 5933, 1<sup>st</sup> paragraph, bottom paragraph).

With regard to claims 19-27, the artisans disclose a primer extension sequencing of a 60-mer DNA template from exon 7 of p53 gene, using the 3'-O-allyl-dUTP-PC-Bodipy-FL-510 nucleotide analog, via use of a polymerase which has been modified (page 5934, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph).

Ruparel et al. disclose that the modified polymerase used in their extension reaction is a 9<sup>th</sup>N polymerase comprising A485L/Y409V mutation (page 5934, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph).

Therefore, Ruparel et al. anticipate the invention as claimed.

Claims 28-30 lack an inventive step under PCT Article 33(3) as being obvious over Ruparel et al. (PNAS, April 26, 2005, Vol. 102, No. 17, pages 5932-5937).

The teachings of Ruparel et al. have already been discussed above.

Ruparel et al. do not explicitly teach their reagents in a kit format.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to package the reagents of Ruparel et al. into a kit for the conventionality of kit in the analytical arts, for providing well-known benefits, such as ready-to-use pre-weighed, purified, and pre-packaged format.

Claims 1-32 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.